

SEQUENCE LISTING

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Carel, Jean-Claude

<120> GPR54 RECEPTOR AGONIST AND ANTAGONIST USEFUL FOR THE TREATMENT OF
GONADOTROPIN RELATED DISEASES

<130> 20990EP

<140> 10/552,028

<141> 2005-10-02

<150> PCT/EP04/004132

<151> 2004-04-02

<150> EP 03290831.1

<151> 2003-04-02

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| atg | cac | acc | gtg | gct | acg | tcc | gga | ccc | aac | gcg | tcc | tgg | ggg | gca | ccg | 48 |
| Met | His | Thr | Val | Ala | Thr | Ser | Gly | Pro | Asn | Ala | Ser | Trp | Gly | Ala | Pro | |
| 1 | | | 5 | | | | | 10 | | | | | 15 | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| gcc | aac | gcc | tcc | ggc | tgc | ccg | ggc | tgt | ggc | gcc | aac | gcc | tcg | gac | ggc | 96 |
| Ala | Asn | Ala | Ser | Gly | Cys | Pro | Gly | Cys | Gly | Ala | Asn | Ala | Ser | Asp | Gly | |
| | | 20 | | | | | 25 | | | | | 30 | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| cca | gtc | cct | tcg | ccg | cgg | gcc | gtg | gac | gcc | tgg | ctc | gtg | ccg | ctc | ttc | 144 |
| Pro | Val | Pro | Ser | Pro | Arg | Ala | Val | Asp | Ala | Trp | Leu | Val | Pro | Leu | Phe | |
| | | 35 | | | | 40 | | | | | 45 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ttc | gcg | gcg | ctg | atg | ctg | ctg | ggc | ctg | gtg | ggg | aac | tcg | ctg | gtc | atc | 192 |
| Phe | Ala | Ala | Leu | Met | Leu | Leu | Gly | Leu | Val | Gly | Asn | Ser | Leu | Val | Ile | |
| | 50 | | | | 55 | | | | | 60 | | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tac | gtc | atc | tgc | cgc | cac | aag | ccg | atg | cgg | acc | gtg | acc | aac | ttc | tac | 240 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

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|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| Tyr 65 | Val | Ile | Cys | Arg | His 70 | Lys | Pro | Met | Arg | Thr 75 | Val | Thr | Asn | Phe | Tyr 80 | |
| atc Ile | gcc Ala | aac Asn | ctg Leu | gcg Ala 85 | gcc Ala | acg Thr | gac Asp | gtg Val | acc Thr 90 | ttc Phe | ctc Leu | ctg Leu | tgc Cys | tgc Cys 95 | gtc Val | 288 |
| ccc Pro | ttc Phe | acg Thr | gcc Ala 100 | ctg Leu | ctg Leu | tac Tyr | ccg Pro | ctg Leu 105 | ccc Pro | ggc Gly | tgg Trp | gtg Val | ctg Leu 110 | ggc Gly | gac Asp | 336 |
| ttc Phe | atg Met | tgc Cys 115 | aag Lys | ttc Phe | gtc Val | aac Asn | tac Tyr 120 | atc Ile | cag Gln | cag Gln | gtc Val | tcg Ser 125 | gtg Val | cag Gln | gcc Ala | 384 |
| acg Thr | tgt Cys 130 | gcc Ala | act Thr | ctg Leu | acc Thr | gcc Ala 135 | atg Met | agt Ser | gtg Val | gac Asp | cgc Arg 140 | tgg Trp | tac Tyr | gtg Val | acg Thr | 432 |
| gtg Val 145 | ttc Phe | ccg Pro | ttg Leu | cgc Arg | gcc Ala 150 | ctg Leu | cac His | cgc Arg | cgc Arg | acg Thr 155 | ccc Pro | cgc Arg | ctg Leu | gcg Ala | ctg Leu 160 | 480 |
| gct Ala | gtc Val | agc Ser | ctc Leu | agc Ser 165 | atc Ile | tgg Trp | gta Val | ggc Gly | tct Ser 170 | gcg Ala | gcg Ala | gtg Val | tct Ser | gcg Ala 175 | ccg Pro | 528 |
| gtg Val | ctc Leu | gcc Ala | ctg Leu 180 | cac His | cgc Arg | ctg Leu | tca Ser | ccc Pro 185 | ggg Gly | ccg Pro | cgc Arg | gcc Ala | tac Tyr 190 | tgc Cys | agt Ser | 576 |
| gag Glu | gcc Ala | ttc Phe 195 | ccc Pro | agc Ser | cgc Arg | gcc Ala | ctg Leu 200 | gag Glu | cgc Arg | gcc Ala | ttc Phe | gca Ala 205 | ctg Leu | tac Tyr | aac Asn | 624 |
| ctg Leu | ctg Leu 210 | gcg Ala | ctg Leu | tac Tyr | ctg Leu | ctg Leu 215 | ccg Pro | ctg Leu | ctc Leu | gcc Ala | acc Thr 220 | tgc Cys | gcc Ala | tgc Cys | tat Tyr | 672 |
| gcg Ala 225 | gcc Ala | atg Met | ctg Leu | cgc Arg | cac His 230 | ctg Leu | ggc Gly | cgg Arg | gtc Val | gcc Ala 235 | gtg Val | cgc Arg | ccc Pro | gcg Ala | ccc Pro 240 | 720 |
| gcc Ala | gat Asp | agc Ser | gcc Ala | ctg Leu 245 | cag Gln | ggg Gly | cag Gln | gtg Val | ctg Leu 250 | gca Ala | gag Glu | cgc Arg | gca Ala | ggc Gly 255 | gcc Ala | 768 |
| gtg Val | cgg Arg | gcc Ala | aag Lys 260 | gtc Val | tcg Ser | cgg Arg | ctg Leu | gtg Val 265 | gcg Ala | gcc Ala | gtg Val | gtc Val | ctg Leu 270 | ctc Leu | ttc Phe | 816 |
| gcc Ala | gcc Ala | tgc Cys 275 | tgg Trp | ggc Gly | ccc Pro | atc Ile | cag Gln 280 | ctg Leu | ttc Phe | ctg Leu | gtg Val | ctg Leu 285 | cag Gln | gcg Ala | ctg Leu | 864 |
| ggc Gly | ccc Pro 290 | gcg Ala | ggc Gly | tcc Ser | tgg Trp | cac His 295 | cca Pro | cgc Arg | agc Ser | tac Tyr | gcc Ala 300 | gcc Ala | tac Tyr | gcg Ala | ctt Leu | 912 |
| aag | acc | tgg | gct | cac | tgc | atg | tcc | tac | agc | aac | tcc | gcg | ctg | aac | ccg | 960 |

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|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------------|------|
| Lys 305 | Thr | Trp | Ala | His | Cys 310 | Met | Ser | Tyr | Ser | Asn 315 | Ser | Ala | Leu | Asn | Pro 320 | |
| ctg Leu | ctc Leu | tac Tyr | gcc Ala | ttc Phe 325 | ctg Leu | ggc Gly | tcg Ser | cac His | ttc Phe 330 | cga Arg | cag Gln | gcc Ala | ttc Phe | cgc Arg 335 | cgc Arg | 1008 |
| gtc Val | tgc Cys | ccc Pro | tgc Cys 340 | gcg Ala | ccg Pro | cgc Arg | cgc Arg | ccc Pro 345 | cgc Arg | cgc Arg | ccc Pro | cgc Arg | cgg Arg 350 | ccc Pro | gga Gly | 1056 |
| ccc Pro | tcg Ser | gac Asp 355 | ccc Pro | gca Ala | gcc Ala | cca Pro | cac His 360 | gcg Ala | gag Glu | ctg Leu | ctc Leu | cgc Arg 365 | ctg Leu | ggg Gly | tcc Ser | 1104 |
| cac His | ccg Pro 370 | gcc Ala | ccc Pro | gcc Ala | agg Arg | gcg Ala 375 | cag Gln | aag Lys | cca Pro | ggg Gly | agc Ser 380 | agt Ser | ggg Gly | ctg Leu | gcc Ala | 1152 |
| gcg Ala 385 | cgc Arg | ggg Gly | ctg Leu | tgc Cys | gtc Val 390 | ctg Leu | ggg Gly | gag Glu | gac Asp | aac Asn 395 | gcc Ala | cct Pro | ctc Leu | tga | | 1197 |

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| Met 1 | His | Thr | Val | Ala 5 | Thr | Ser | Gly | Pro | Asn 10 | Ala | Ser | Trp | Gly | Ala 15 | Pro |
|----------|-----|-----|-----|----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|

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|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|
| Ala | Asn | Ala | Ser 20 | Gly | Cys | Pro | Gly | Cys 25 | Gly | Ala | Asn | Ala | Ser 30 | Asp | Gly |
|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|

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|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|
| Pro | Val | Pro 35 | Ser | Pro | Arg | Ala | Val 40 | Asp | Ala | Trp | Leu | Val 45 | Pro | Leu | Phe |
|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|

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|-----------|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|
| Phe 50 | Ala | Ala | Leu | Met | Leu | Leu 55 | Gly | Leu | Val | Gly | Asn 60 | Ser | Leu | Val | Ile |
|-----------|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|

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| Tyr 65 | Val | Ile | Cys | Arg | His 70 | Lys | Pro | Met | Arg | Thr 75 | Val | Thr | Asn | Phe | Tyr 80 |
|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|

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|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|
| Ile | Ala | Asn | Leu | Ala 85 | Ala | Thr | Asp | Val | Thr 90 | Phe | Leu | Leu | Cys | Cys 95 | Val |
|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|

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|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|
| Pro | Phe | Thr | Ala 100 | Leu | Leu | Tyr | Pro | Leu 105 | Pro | Gly | Trp | Val | Leu 110 | Gly | Asp |
|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Met | Cys | Lys | Phe | Val | Asn | Tyr | Ile | Gln | Gln | Val | Ser | Val | Gln | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

| 115 | | | | | 120 | | | | | 125 | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Cys | Ala | Thr | Leu | Thr | Ala | Met | Ser | Val | Asp | Arg | Trp | Tyr | Val | Thr |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Val | Phe | Pro | Leu | Arg | Ala | Leu | His | Arg | Arg | Thr | Pro | Arg | Leu | Ala | Leu |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ala | Val | Ser | Leu | Ser | Ile | Trp | Val | Gly | Ser | Ala | Ala | Val | Ser | Ala | Pro |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Val | Leu | Ala | Leu | His | Arg | Leu | Ser | Pro | Gly | Pro | Arg | Ala | Tyr | Cys | Ser |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Glu | Ala | Phe | Pro | Ser | Arg | Ala | Leu | Glu | Arg | Ala | Phe | Ala | Leu | Tyr | Asn |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Leu | Leu | Ala | Leu | Tyr | Leu | Leu | Pro | Leu | Leu | Ala | Thr | Cys | Ala | Cys | Tyr |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Ala | Ala | Met | Leu | Arg | His | Leu | Gly | Arg | Val | Ala | Val | Arg | Pro | Ala | Pro |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Ala | Asp | Ser | Ala | Leu | Gln | Gly | Gln | Val | Leu | Ala | Glu | Arg | Ala | Gly | Ala |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Val | Arg | Ala | Lys | Val | Ser | Arg | Leu | Val | Ala | Ala | Val | Val | Leu | Leu | Phe |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Ala | Ala | Cys | Trp | Gly | Pro | Ile | Gln | Leu | Phe | Leu | Val | Leu | Gln | Ala | Leu |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Gly | Pro | Ala | Gly | Ser | Trp | His | Pro | Arg | Ser | Tyr | Ala | Ala | Tyr | Ala | Leu |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Lys | Thr | Trp | Ala | His | Cys | Met | Ser | Tyr | Ser | Asn | Ser | Ala | Leu | Asn | Pro |
| 305 | | | | | 310 | | | | | 315 | | | | 320 | |
| Leu | Leu | Tyr | Ala | Phe | Leu | Gly | Ser | His | Phe | Arg | Gln | Ala | Phe | Arg | Arg |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Val | Cys | Pro | Cys | Ala | Pro | Arg | Arg | Pro | Arg | Arg | Pro | Arg | Arg | Pro | Gly |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Pro | Ser | Asp | Pro | Ala | Ala | Pro | His | Ala | Glu | Leu | Leu | Arg | Leu | Gly | Ser |

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 370 375 380
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 Pro Val Pro Ser Pro Arg Ala Val Asp Ala Trp Leu Val Pro Leu Phe
 35 40 45
 Phe Ala Ala Leu Met Leu Leu Gly Leu Val Gly Asn Ser Leu Val Ile
 50 55 60
 Tyr Val Ile Cys Arg His Lys Pro Met Arg Thr Val Thr Asn Phe Tyr
 65 70 75 80
 Ile Ala Asn Leu Ala Ala Thr Asp Val Thr Phe Leu Leu Cys Cys Val
 85 90 95
 Pro Phe Thr Ala Leu Leu Tyr Pro Leu Pro Gly Trp Val Leu Gly Asp
 100 105 110
 Phe Met Cys Lys Phe Val Asn Tyr Ile Gln Gln Val Ser Val Gln Ala
 115 120 125
 Thr Cys Ala Thr Leu Thr Ala Met Ser Val Asp Arg Trp Tyr Val Thr
 130 135 140
 Val Phe Pro Leu Arg Ala Leu His Arg Arg Thr Pro Arg Leu Ala Leu
 145 150 155 160
 Ala Val Ser Leu Ser Ile Trp Val Gly Ser Ala Ala Val Ser Ala Pro
 165 170 175

Val Leu Ala Leu His Arg Leu Ser Pro Gly Pro Arg Ala Tyr Cys Ser
 180 185 190
 Glu Ala Phe Pro Ser Arg Ala Leu Glu Arg Ala Phe Ala Leu Tyr Asn
 195 200 205
 Leu Leu Ala Leu Tyr Leu Leu Pro Leu Leu Ala Thr Cys Ala Cys Tyr
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 Ala Ala Met Leu Arg His Leu Gly Arg Val Ala Val Arg Pro Ala Pro
 225 230 235 240
 Ala Asp Ser Ala Leu Gln Gly Gln Val Leu Ala Glu Arg Ala Gly Ala
 245 250 255
 Val Arg Ala Lys Val Ser Arg Leu Val Ala Ala Val Val Leu Leu Phe
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 Ala Ala Cys Trp Gly Pro Ile Gln Leu Phe Leu Val Leu Gln Ala Leu
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 Gly Pro Ala Gly Ser Trp His Pro Arg Ser Tyr Ala Ala Tyr Ala Leu
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 Lys Thr Trp Ala His Cys Met Ser Tyr Ser Asn Ser Ala Leu Asn Pro
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 Leu Leu Tyr Ala Phe Leu Gly Ser His Phe Arg Gln Ala Phe Arg Arg
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 Val Cys Pro Cys Ala Pro Arg Arg Pro Arg Arg Pro Arg Arg Pro Gly
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 355 360 365
 His Pro Ala Pro Ala Arg Ala Gln Lys Pro Gly Ser Ser Gly Leu Ala
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 Ala Arg Gly Leu Cys Val Leu Gly Glu Asp Asn Ala Pro Leu
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